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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/644,387	08/23/2000	Gregory E. Agoston	05213-0541	1513

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EXAMINER
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BADIO, BARBARA P

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 01/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/644,387

Applicant(s)

AGOSTON ET AL.

Examiner

Barbara P Badio, Ph.D.

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☐ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 14-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-13 and 21-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                            | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____   |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)        | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ | 6) <input type="checkbox"/> Other:  |

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**Final Office Action on the Merits**

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 102***

2. The rejections of claims 1-13 and 21-25 under 35 USC 102(b) over (a) D'Amato et al. ('074); (b) Clark et al. ('168) and (c) Fotsis et al. ('900) are maintained.

Applicant argues that the references do not describe how the 2-methoxyestradiol was made nor provide any information as to the source of the 2-methoxyestradiol employed in the experiments described therein. Thus, it can be fairly concluded that the source was commercial and it cannot be assumed that the compound was pure. Applicant's argument was considered but not persuasive for the following reasons.

The reference teaches that chemical synthesis of estradiol is known in the art (see for example, '074, col. 5, lines 38-54). However, the issue is not whether the reference teaches how to make the compound but whether the prior art compound reads on the claimed compound. The assumption is that the compound taught by the prior art is pure and applicant has not provided evidence of record contrary to said assumption.

Even if one assumes the source of the compound was commercial, as indicated by the data sheet from Sigma, the compound can be obtained in greater than 99.5% purity as determined by TLC (see Exhibit A).

For these reasons and those given in Paper No.10, the rejections of claims 1-13 and 21-25 under 35 USC 102(b) over (a) D'Amato et al. ('074); (b) Clark et al. ('168) and (c) Fotsis et al. ('900) are maintained.

**3. The rejection of claims 1-13 and 21-25 under 35 USC 102(e) over Stewart et al. ('966) is maintained.**

Applicant argues that the compound utilized by Stewart as determined by HPLC was only 98% pure and for therapeutic use in humans a high level of purity is required. Applicant's argument was considered but not persuasive for the following reason.

The certificate of analysis of 2-methoxyestradiol from Sigma indicates (a) the **minimum** purity by HPLC is 98% and (b) purity by TLC was >99.5%. Therefore, the claimed compound and that utilized by Stewart and commercially availability at the time of the present application are identical.

For this reason and those given in Paper No.10, the rejection of claims 1-13 and 21-25 under 35 USC 102(b) over Stewart et al. ('966) is maintained.

***Claim Rejections - 35 USC § 103***

**4. The rejection of claims 1-13 and 21-25 under 35 USC 103(a) over D'Amato et al. ('074), Clark et al. ('168), Fotsis et al. ('900) or Stewart ('966) is maintained.**

Applicant argues that even if it is obvious to purify compounds for pharmaceutical applications that the degree of purity of the active compound and/or which impurities should be removed from the active compound is not obvious. Applicant also argues that the certificate of analysis data sheet from Sigma refutes the examiner's position that the ordinary artisan would expect the compound to be in pure form and that the prior art does not teach a composition containing less than 0.03 % estradiol, etc. Applicant's argument was considered but not persuasive for the following reasons.

As indicated above in #3, the certificate of analysis data of 2-methoxyestradiol from Sigma indicates (a) the **minimum** purity by HPLC is 98% and (b) purity by TLC was >99.5%. Thus, before the claimed invention, 2-methoxyestradiol having a purity of 98 to >99.5% was known in the art as evidenced by the data sheet.

Purification of compounds to use as pharmaceutical agents involves obtaining a compound containing as close to zero percent impurities as possible. Although, there are some impurities that are more harmful than others, the goal in the pharmaceutical art is to obtain a pure compound with little or no impurities that would be harmful to the patient. It would also take only routine experimentation to determine which impurity is more harmful. Therefore, obtaining a compound containing as little as possible of that impurity would be obvious to the skilled artisan.

Lastly, applicant argues that none of the references teach the composition containing less than 0.03% estradiol, etc. It is noted that the phrase "less than" implies that said compound may be absent. Therefore, the prior art compound does not have to contain any of the other compounds recited by applicant. In addition, because the

reference is silent as to the presence of other compounds does not imply that they are not present. Applicant has not provided any evidence of record that these compound are not present in the compound of Sigma or any of the other prior art compositions containing 2-methoxyestradiol.

For these reasons and those given in Paper No. 10, the rejection of claims 1-13 and 21-25 under 35 USC 103(a) over D'Amato et al. ('074), Clark et al. ('168), Fotsis et al. ('900) or Stewart ('966) is maintained.

### ***Conclusion***

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

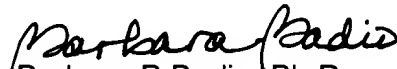
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***Telephon Inquiry***

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P Badio, Ph.D. whose telephone number is 703-308-4595. The examiner can normally be reached on M-F from 7:30am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

  
Barbara P Badio, Ph.D.  
Primary Examiner  
Art Unit 1616

BB  
January 31, 2002